

Principles of Pluripotency

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Pluripotency is the capacity of an individual cell to produce all lineages of the mature organism including the germline in response to extrinsic cues. In mice and rats this naïve state at the foundation of mammalian development can be captured in culture in the form of self-renewing embryonic stem (ES) cells. ES cells cultured in serum are highly mosaic and appear metastable. More homogenous propagation is achieved using two selective kinase inhibitors that target the mitogen-activated protein kinase (Erk) cascade and glycogen synthase kinase-3 (Gsk3) respectively. We have suggested that ES cells maintained using the two inhibitors (2i) along with the cytokine leukaemia inhibitory factor (LIF) are anchored in a self-renewing ground state. The transcription factor hub that sustains naïve pluripotency is increasingly well-defined. The next challenge is to elucidate how ES cells exit the ground state and enter into multi-lineage commitment and differentiation.

Our research is supported by The Wellcome Trust, the Medical Research Council, the Biotechnology and Biological Sciences Research Council, and the European Commission Framework 7 Program.